amendments.

83. A transgenic mouse comprising in its germline a modified genome wherein said modification comprises inactivated endogenous immunoglobulin heavy chain loci in which all of the J segment genes from both copies of the immunoglobulin heavy chain locus are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin heavy chain from the inactivated loci.

84. The mouse of claim 83 wherein said modification further comprises an inactivated endogenous immunoglobulin light chain locus in which all of the J segment genes from at least one copy of an immunoglobulin light chain locus are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin light chain from the inactivated locus.

85. The mouse of claim 83 wherein said modification comprises inactivated endogenous immunoglobulin light chain loci in which all of the J segment genes from both copies of the immunoglobulin light chain locus are deleted to prevent rearrangement and to prevent formation of a transcript of a rearranged locus and the expression of an endogenous immunoglobulin light chain from the inactivated loci.

86. The mouse of claim 83 ~~wherein said modification~~ further comprises ~~inclusion~~ of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

87. The mouse of claim 84 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

88. The mouse of claim 85 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence identical to the germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J

segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

C1

95. The transgenic mouse of claim 86 wherein the xenogeneic light chain immunoglobulin locus is human.

C2

96. The transgenic mouse of claim 87 wherein the xenogeneic light chain immunoglobulin locus is human.

97. The transgenic mouse of claim 88 wherein the xenogeneic light chain immunoglobulin locus is human.

104. The mouse of claim 83 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

C3

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

105. The mouse of claim 84 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or

~~xenogeneic heavy chain or both;~~

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

106. The mouse of claim 85 wherein said modification further comprises inclusion of, in said genome, an immunoglobulin locus encoding a xenogeneic light chain or xenogeneic heavy chain or both;

wherein said xenogeneic heavy chain comprises a DNA sequence that is derived from and contains a germline DNA sequence of human chromosome 14 from the D segment genes of the human immunoglobulin heavy chain locus, continuing through the J segment genes and the constant region genes through Cμ of that locus, wherein said DNA sequence does not include a gamma constant region, and wherein said DNA fragment is operably linked to at least one human V segment gene found on human chromosome 14.

107. The transgenic mouse of claim 86 wherein the xenogeneic light chain immunoglobulin locus is human.

108. The transgenic mouse of claim 87 wherein the xenogeneic light chain immunoglobulin locus is human.

109. The transgenic mouse of claim 88 wherein the